

Remarks

Claims 2-6 and 74-78 are pending in this application upon the entry of the amendments presented herein. Claims 1, 7-8, and 32-43 are canceled without prejudice to Applicants' right to pursue the subject matter recited by them in one or more divisional, continuation or continuation-in-part applications.

Claims 2 and 4 are amended to replace the term "not racemic" with the term "stereomerically pure." Support for the amendments can be found, for example, on pages 13-15 of the specification.

New claims 74-78 are added to recite, in part, pharmaceutical compositions comprising the compounds recited by claims 2-6. Support can be found, for example, on page 16, lines 8-12 of the specification. No new matter has been introduced.

Applicants respectfully submit that all of the pending claims are allowable for at least the following reasons.

A. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 2-3 of the Office Action, the rejection of claims 1-8 and 32-43 under 35 U.S.C. § 103, as allegedly obvious over Jeffery *et al.*, *J. Chem. Soc., Perkin Trans.*, 1: 2583-9 (1996) ("Jeffery") and Fang *et al.*, *Tetrahedron: Asymmetry*, 10: 4477-4480 (1999) ("Fang") is maintained. Applicants respectfully traverse this rejection.

Applicants respectfully point out that a *prima facie* of obviousness cannot be established by Jeffery and Fang because: 1) Jeffery and Fang fail to teach or suggest all of the limitations of the pending claims; and 2) there would have been no motivation for those of ordinary skill in the art to make and use the claimed compounds because neither reference suggests the desirability of the claimed compounds.

First, it is clear that Jeffery fails to teach the claimed compounds. To the extent that the Examiner relies on Compounds 4 and 5a of Jeffery, Applicants respectfully point out that those compounds depict racemic mixtures, and thus, are not stereomerically pure, as recited by the pending claims.

To be specific, Applicants respectfully point out that Compound 4 of Jeffery, which corresponds to 1-hydroxy derivatives of sibutramine, is clearly a

depiction of a racemic mixture, as evidenced by the absence of any “positional denotation” of the chemical bonds.

In addition, Compound 5a (7-hydroxy derivatives of sibutramine), although showing “positional denotation” of certain chemical bonds, also does not show stereomerically pure compounds. This is because Compound 5a does not show any “positional denotation” of any of the chemical bonds connected to chiral carbon atoms, *i.e.*, carbon atoms at 2- and 4-positions. As Applicants have pointed out, Compound 5a merely shows cis/trans isomerism of the groups attached to carbon atoms at 5- and 7-positions in relation to the cyclobutyl ring, but it does not show a stereomerically pure isomer or any stereo-chemistry at the chiral center of the compound. In other words, Jeffery merely discloses racemic mixture of the compounds it discloses, but is completely silent about the stereoisomerism of those compounds.

In addition, Jeffery would not have provided to those of ordinary skill in the art any suggestion whatsoever regarding the claimed compounds. In fact, Jeffery actively teaches away from the claimed invention by providing that the pharmacological activity of sibutramine is “mediated *predominantly by*” two demethylated amines of sibutramine (Compounds 2 and 3), which are not recited by the pending claims.

Fang does not cure this deficiency because Fang also does not teach or suggest the claimed compounds. Fang merely discloses the enantiomers of sibutramine and desmethylsibutramine. Thus, it is clear that Fang does not teach the claimed compounds. Further, Fang does not suggest the claimed compounds because it does not disclose that the methods disclosed therein may be used for the preparation of other compounds, much less for the compounds claimed herein. Therefore, the combination of Jeffery and Fang fails to teach or suggest all of the limitations of the pending claims. For this reason alone, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

Furthermore, there would have been no motivation to combine or modify Jeffery and Fang. It is well-established that prior art must provide the motivation to combine or modify to establish a *prima facie* case of obviousness. (*See Noelle*, 355 F.3d 1343, 1352 (Fed. Cir. 2004) (“the suggestion … ‘must be founded in the prior art, not in the applicant’s disclosure.’” (quoting *In re Vaeck*, 947 F.2d 488,

493 (Fed. Cir. 1991))). However, neither Jeffery nor Fang provides the required motivation because there is no suggestion whatsoever in either references, or in any other prior art of record, that combining the two references to make and use the claimed compounds would be advantageous.²

Despite this fact, it appears that, while the Examiner recognizes that Jeffery does not disclose the claimed optical isomers, the Examiner rejects the pending claims based solely on the allegation that a “stereoisomer is *prima facie* obvious over racemate, as a whole, absent evidence to the contrary.” (Office Action, page 3). The Examiner cites to three cases (*i.e.*, *In re Adamson*, *Brenner v. Ladd*, and *In re Williams*) to support this proposition. Applicants respectfully point out that the Examiner’s position is based on faulty legal principles, which are directly contrary to the well-settled legal principles concerning stereoisomers.

In this regard, Applicants again respectfully invite the Examiner’s attention to *In re Holy*, 2004 WL 77012 (B.P.A.I. 2004), a copy of which was provided in Applicants’ Response dated May 19, 2006. In *Holy*, claims at issue recited a genus of enantiomerically pure chemical compounds. The claims were rejected under 35 U.S.C. § 103 over, among others, a reference which disclosed a racemic mixture of a compound encompassed by the chemical structure recited by the claims. (*See Holy*, page *3). The examiner in *Holy*, rejected the claims as allegedly obvious, citing *In re Adamson* and providing a reasoning substantially identical to that provided in the present application by the Examiner, *i.e.*, that an optical isomer is *prima facie* obvious over prior disclosure of its racemic mixture. (*See id.*).

In reversing the examiner’s rejection, the Board stated that:

[i]n order to make a *prima facie* case of obviousness based on the structural similarity, in this case similarity between the claimed optical isomer and its racemate taught by the prior art, not only must the structural similarity exist, but the prior art must also provide reason or motivation to make the claimed compound.

² Indeed, Applicants respectfully point out that even if the two references are combined, those of ordinary skill in the art would not have arrived at the present invention because the combination fails to teach or suggest all of the claim limitations, as discussed above.

(*Id.* at page *4 (citing *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990); *In re Mayne*, 104 F.3d 1339, 1341 (Fed. Cir. 1997); and *In re Payne*, 606 F.2d 303, 313 (C.C.P.A. 1979)) (emphasis added)).

The Board went on to hold that the rejection cannot be sustained because the references cited by the examiner in *Holy* did not provide any motivation, and the examiner did not “set forth any facts or findings to support the motivational statement, especially since all that is currently being claimed is a single isomer.” (*Id.* (citing *In re Lee*, 277 F.3d 1338, 1343-4 (Fed. Cir. 2002)) (emphasis added)).

Further, in addressing the examiner’s reliance on *Adamson* “for the proposition that an optically pure form of a compound is *per se* obvious over a disclosure of a racemic mixture of the compound,” the Board held that such reliance is misplaced because “one cannot rely on case alone ... to provide the motivation to modify a prior art compound.” (*Id.* at page *6 (emphasis added)). The Board further stated that the question is “whether there is something in the prior art as a whole to suggest the desirability... of making the combination,” and held that the rejection should be reversed in view of the teaching away from making the modification suggested by the examiner.³ (*Id.* (citing *In re Rouffet*, 149 F.3d 1350, 1356 (Fed. Cir. 1998))).

As can be seen, the facts and holdings of *Holy* are directly applicable to the present application. As in *Holy*, the Examiner’s rejection is based solely on the allegation that a stereoisomer is *prima facie* obvious over the prior disclosure of its racemate. As in *Holy*, the Examiner relies solely on cases to provide support for his allegation, without any consideration as to whether prior art as a whole would have provided any motivation. As in *Holy*, the Examiner does not provide any evidence or reasoning to rebut the teaching away pointed out by Applicants. Therefore, Applicants respectfully submit that the rejection of the claims 35 U.S.C. § 103 cannot be sustained.

³ The applicant in *Holy* provided references that taught that the racemic compound disclosed in the reference cited by the examiner is an inactive product, and pointed out that the prior art as a whole taught away from the claimed stereoisomer. (*See Holy*, page *5). This is virtually identical to Applicants’ submission that Jeffery teaches away from the claimed invention. (*See Applicants’ Response of September 28, 2005*, page 3). The Examiner does not provide any evidence or reasoning to rebut this submission.

Conclusion

In sum, Applicants respectfully submit that: 1) Jeffery and Fang fail to establish a *prima facie* case of obviousness; 2) a *prima facie* case of obviousness also cannot be established in view of the teaching away by Jeffery's disclosure; and 3) the Examiner's reasoning in support of the rejection under 35 U.S.C. § 103 is legally faulty. For at least the foregoing reasons, Applicants respectfully submit that all of the pending claims are allowable, and request that the rejection of the claims be withdrawn.

No fee is believed due for this submission. Should any additional fees be due for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

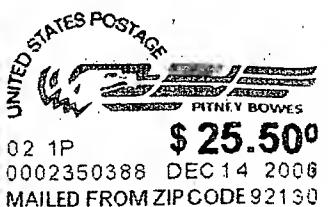
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